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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,466	06/20/2001	Arthur L. Herbst	58532-012	9630

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EXAMINER	
KIM, VICKIE Y	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 05/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/884,466	HERBST ET AL.	
	Examiner	Art Unit	
	Vickie Kim	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-26* is/are pending in the application.

4a) Of the above claim(s) *16 and 18-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-15,17 and 23-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicant's response filed 1/29/04.

2. Applicant's affirmation of election of species, fatigue, is acknowledged and the claims 13-15, 17 and 23-26 are presented for the examination.

Response to Arguments

3. Applicant's arguments filed 1/29/04 have been fully considered but they are not persuasive.

4. In response to applicant's argument that Collins et al(US'728) , Kutilek III et al(US '217) ,Wilder (US'421), Bull et al(US'145) and Shafran (US'015) are not pertinent to the claimed subject matter because they fail to teach the use of selective COX II inhibitors for treating radiation induced fatigue. Applicant is reminded that the examiner's allegation is made based on obviousness that can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the primary teaching of Collin et al, as teaching that a COX II inhibitor is effectively used for treating IL-1 mediated inflammatory diseases such as side effects of radiation therapy, chronic fatigue syndrome. This case is prima facie obvious because secondary references teach the fatigue is most common side effect associated with radiation therapy(Kutilek

US'2317), fatigue is sign and symptom of inflammation that can be corrected by treating inflammation(Bull US'145). Thus, applicant's invention(i.e. the use of COX II inhibitors for treating radiation induced fatigue) is readily apparent when these references are combined together because the teaching, suggestion, and motivation are found in the references.

Additionally, Wilder(US'421), as teaching that the COX-II inhibitors are effectively used in the treatment of photodamages(toxicities) including weakness due to radiation(i.e.UV) and Safran(US'015), as teaching that COX-2 inhibitors are effectively used in fatigue that is a side effect associated with antibiotic therapy, are pertinent enough to motivate one of ordinary skill in the art to select the COX II inhibitors as the drug of the choice for fatigue treatment and one would have reasonably expected the successful result regardless the etiology of fatigue condition.

5. In the response applicant's argument that the examiner's allegation(i.e. well known knowledge that fatigue associated with radiation therapy is mediated by inflammatory process) lacks evidence and thus, the examiner's conclusion(i.e. the combination of cited prior art renders the use of COX II inhibitors to treat fatigue associated with radiation treatment obvious) is disagreed, whereas applicant states, by quoting author's suggestion(in the state of the art), as such that anemia is a likely common source of fatigue in radiation therapy.

Applicants are reminded that applicants propose that a component of radiation induced fatigue is mediated by the inflammatory response, see instant specification at page 4, paragraph 19.

Applicants' argument is self contradicting to his own teaching and is not persuasive. This examiner agreed that the etiology(causes) of fatigue may not be unknown but at the time of applicants' invention was made, the inflammatory process could have been believed to be the mechanism of the action(mediated by) responsible for fatigue symptoms regardless its etiologies.

Any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning(an explicit teaching is lacking). But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Applicants argument is not persuasive for the reasons above, and the rejection is maintained as stated in the previous office action. The copy of the 103 rejection is as follows.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 13-15, 17 and 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Collins et al (US 6096728) in view of Kutilek, III et al(US 5,770,217) ,Wilder (US 2002/0009421), Bull et al(US5506145) and Shafran (US 6,297,015).

Collins et al (US'728 hereafter) teach a composition comprising COX2 inhibitor such as celecoxib used in the treatment of acute or chronic inflammatory diseases including chronic fatigue syndrome or side effects from radiation therapy, see column 1, line 57, column 2, line 3 and column 32, lines 21-34.

Although US'728 does not specifically teach the fatigue as the specific species of said side effects(US'728) from radiation therapy, it would have been, however, obvious to one of ordinary skill in the art to extend the teaching of US'728 at the time of the invention was made to apply not only to chronic fatigue syndrome but also to fatigue that is a side effect induced by radiation when Collins et al is modified with Wilder, Bull and Shoran's teaching because each patentee teaches a piece of information that remedies the deficiency of US'728.

It is commonly known to any skilled artisan that fatigue is mediated by inflammatory process and also induced by radiation exposure known as a common side effect from radiation therapy.

The said conventional knowledge is as evidenced by numerous prior art references including applicants own admission (see instant specification at page 4, paragraph 19 and see also references in PTO-892 enclosed).

For instance, Kutilek, III et al(US'217 hereafter) teach a fatigue is a side effect that is so commonly associated with radiation/chemo-therapy, see column 16, lines 39-43 and column 3, lines 56-63. Although the invention of US'217 is not relevant to the instant invention, it is cited because it has the literal support on the allegation this examiner made. Bull et al(US'145 hereafter) teaches that fatigue, fever chills are signs

and symptoms of inflammation wherein the treatment of said signs and symptoms can be corrected by treating inflammation, see column 1,lines 32-45.

Meanwhile, Wilder et al(US421) and Shafran et al(US'015) teach the effectivenss of COX-2 inhibitors and its use in the treatment against not only radiation induced inflammation but also fatigue or other symptoms and signs such as fever and chills as well.

Wilder et al (US'421, hereafter) teach an effective treatment of UV radiation induced photodamages to the skin and symptoms related thereto such as inflammation, weakness, chills, fever, pain and tenderness, using a therapeutically effective amount of COX-2 inhibitors such as celecoxib or rofecoxib, see full text, especially paragraphs 28-31 at column 4. The effective dosage regimen for the topical application of COX-2 inhibitor is about 50-400mg per unit dosage, preferably 100-200mg in suspension or solution, see paragraphs 34-35 at column 4.

Shafran et al (US'015 hereafter) teach a COX-2 inhibitor such as celecoxib and its use in the treatment of side effects such as fatigue, fever, and chills associated with rifabutin and macrolide(e.g. clarithromycin) antibiotic therapy(RMAT) used in treating crohn's disease, see column 5, lines 60 thru column 6, lines 18. US'015 teaches that the symptoms(e.g. fatigue) is responded well to COX-2 inhibitor such as celecoxib with 200mg /per day with no adverse effects.

Thus, it would have been obvious to one of ordinary skill in the art to use COX-2 inhibitors to treat radiation induced fatigue when these references are combined because the successful result for the treatment of radiation induced fatigue by COX-2

inhibitor is readily apparent to any skilled artisan as well as other acute or chronic fatigues regardless of its pathologies where reasonable expectation of success would flow naturally from following the suggestion of the prior art.

One would have been motivated to make such modification because COX-2 inhibitor's selective inhibitory activity would allow less undesirable side effect and is desirable than other non-steroidal anti-inflammatory drugs (NSAID) due to its therapeutic superiority. One would have been motivated to combine these references because the teachings are reasonably pertinent to the particular problem with which the applicant was concerned. Furthermore, it is always desired to have extended therapeutic modalities that would increase patient's compliance because patient's selection would be made on individual's need and preference, which would eventually have improved the overall quality of the treatment and increase the industrial value.

Conclusion

3. No claim is allowed.

4. It is noted that there are several documents pertinent to the claimed subject matter cited in PTO-892 which also supports this examiner's allegation(i.e. radiation induced fatigue mediated by inflammatory process is well known in the art).

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vickie Kim whose telephone number is 703-305-1675. The examiner can normally be reached on Tuesday-Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel can be reached on 703-308-4725. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-3165 for regular communications and 703-746-3165 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

VICKIE KIM
PRIMARY EXAMINER

Vickie Kim,
Primary Patent Examiner
Art unit 1614